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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/532,948	01/09/2006	Shigeyuki Yokoyama	P/2850-106	2037

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EXAMINER	
GEBREYESUS, KAGNEW H	
ART UNIT	PAPER NUMBER
1656	
MAIL DATE	DELIVERY MODE
08/07/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/532,948	YOKOYAMA ET AL.	
	Examiner	Art Unit	
	KAGNEW H. GEBREYESUS	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 6-16* is/are pending in the application.

4a) Of the above claim(s) *8-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 6 and 7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response on April 30, 2008 to the Office Action dated November 14, 2007 is acknowledged. Applicants have amended claims 1, 6 and 7. Claims 1, 6-16 are pending. Claims 8-16 have been withdrawn as being part of non-elected claims. This election is made final. Claims 1, 6 and 7 are present for examination.

Withdrawn - Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1, 6 and 7 were rejected under 35 U.S.C. 101 because the claimed inventions are directed to non-statutory subject matter. As broadly interpreted, the claims contained embodiments that encompass producing proteins in cells within a multi-cellular organism including humans. This rejection is withdrawn following amendment to the claims.

Withdrawn - Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 6 and 7 were rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method expressing a protein comprising a non-

naturally occurring amino acid comprising expressing said protein in an isolated animal cell, does not reasonably provide enablement for a method of expressing a protein comprising a non-naturally occurring amino acid in an animal cell wherein said cell can be in any animal including humans. Applicants have amended the claims to recite isolated cells. This rejection has been withdrawn.

Maintained -Claim Rejections - 35 USC § 103

Claims 1, 6 and 7 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Kiga et al (An Engineered Escherichia coli tyrosyl-tRNA synthetase for Site Specific incorporation of an unnatural amino acid into proteins in Eukaryotic translation and its application in wheat germ cell-free systems. PNAS July 23, 2002).

Kiga et al teach tyrosyl tRNA from Escherichia coli (E. coli) was engineered to preferentially recognize 3-iodo-L-tyrosine rather than L-tyrosine for the site-specific incorporation of 3-iodo-L-tyrosine into proteins in eukaryotic translation systems.

Applicant's response argues:

"…To begin with, the tRNA and aminoacyl tRNA synthetase have coevolved and, therefore, each said molecule has a shape and characteristics which are influential to the other. For example, the tyrosine tRNA molecules from *E. coli* and *B. stearothermophilus* are as different from each other as are the tyrosyl-tRNA synthetases from these organisms. Further to the above, compatibility of a tRNA from one species with the corresponding tRNA from a different species cannot be predicted, i.e., it must be experimentally tested. In other words, such compatibility cannot be understood *a priori.*

Applicant's argument has been carefully considered but not found persuasive because in paragraph [0074] the specification discloses:

"…B. stearothermophilus suppressor tRNA.sup.Tyr was cloned to a vector for its introduction into animal cells without any alterations. It was, in fact, expressed in animal cells (refer to the examples described later), and exhibited suppression activity when combined with the aforementioned E. coli TyrRS (refer to the examples to be described later)…"

Furthermore the specification teaches that the reason why *Bacillus stearothermophilus* tRNA.sup.Tyr functions in Eukaryotic cells is because tRNA.sup.Tyr from *Bacillus stearothermophilus*, originally has box B and box A within its sequence which allows it to be expressed in eukaryotes without any alterations.

The specification further teaches SEQ ID NO: 1, an artificial sequence consisting of a leader sequence of human tRNA gene, the tRNA.sup.Tyr gene of *B. stearothermophilus* comprising a CUA anticodon any without the terminal CCA sequence and a transcription terminator in this codon. This artificial sequence was used with the *E. coli* mutant tRNA synthetase (V37C195) to incorporate iodotyrosine (see In paragraph [0101]). However the specification does not teach co-evolving the tRNA from Bacillus as alleged in Applicants argument.

Furthermore the response argues:

The Kiga reference cited to reject the claims only discloses that a combination of tRNA synthetase and tRNA from *E. coli* might be used in an animal cell. The reference neither teaches nor suggests, however, to use a combination of tRNA synthetase and tRNA from different species for use in expressing peptides in isolated animal cells as is presently claimed.

Applicant's claims are drawn to a method that uses mutant tRNA synthetase (V37C195) from *E. coli* and suppressor tRNA **originating in** *Bacillus stearothermophilus* capable of binding with the tyrosine derivative in the presence of mutant tyrosyl tRNA synthetase without disclosing any structure for the particular suppressor tRNA used in the method. However when broadly interpreted, a suppressor tRNA originating in *Bacillus stearothermophilus* can encompass any variation in sequence structure including a structure identical to Kiga et al's suppressor tRNA from *E. coli.* Kiga et al have shown a method of producing a protein comprising the unnatural amino acid 3-iodo-L-tyrosine using the *E. coli* V37C195 mutant tRNA synthetase (ORS) and an amber suppressor tRNA from *E. coli* in a Eukaryotic translation system (see fig. 2, lane 3).

Kiga et al's method is a cell free system that does not require transfecting vectors into a eukaryotic cell thus provides evidence that the *E. coli* amber suppressor tRNA can function with the V37C195 mutant tRNA synthetase from *E. coli* in Eukaryotic cells. Therefore claims 1, 6 and 7 remain rejected under 35 U.S.C. 103(a) as being obvious over Kiga et al.

This action is a **final rejection** and is intended to close the prosecution of this application. Applicant's reply under 37 CFR 1.113 to this action is limited either to an appeal to the Board of Patent Appeals and Interferences or to an amendment complying with the requirements set forth below.

If applicant should desire to appeal any rejection made by the examiner, a Notice of Appeal must be filed within the period for reply identifying the rejected claim or claims appealed.

If applicant should desire to file an amendment, entry of a proposed amendment after final rejection cannot be made as a matter of right unless it merely cancels claims or complies with a formal requirement made earlier. Amendments touching the merits of the application which otherwise might not be proper may be admitted upon a showing a good and sufficient reasons why they are necessary and why they were not presented earlier.

A reply under 37 CFR 1.113 to a final rejection must include the appeal from, or cancellation of, each rejected claim. The filing of an amendment after final rejection, whether or not it is entered, does not stop the running of the statutory period for reply to the final rejection unless the examiner holds the claims to be in condition for allowance. Accordingly, if a Notice of Appeal has not been filed properly within the period for reply, or any extension of this period obtained under either 37 CFR 1.136(a) or (b), the application will become abandoned.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kagnew H. Gebreyesus whose telephone number is 571-272-2937. The examiner can normally be reached on 8:30am-5: 30pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.
Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you

have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kagnew H Gebreyesus PhD/
Examiner, Art Unit 1656
August 5, 2008.
KHG

/Kathleen Kerr Bragdon/
Supervisory Patent Examiner, Art Unit 1656